
# RESPONSE TO THERAPEUTIC TREATMENT IN HIV-INFECTED CHILDREN

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There are a total of 92 Ministry of Health and CHAM (Christian Health Association of Malawi) NRU across Malawi, 70 of which are currently being supported by non governmental organisations (NGOs) in the implementation of the national protocols for the treatment of severe malnutrition; 48 of these are supported by the ACF International Network.

At the time the ACF International Network started supporting the NRU, the standard Malawi National protocols in place were adapted from the WHO guidelines which are inpatient based and use F75 and F100 therapeutic milk. These protocols are under review and the new national guidelines will have a community and outpatient focus, following a 'CTC' (Community Therapeutic Care) model[32].

The current WHO treatment protocols for severe acute malnourished children have not been assessed on appropriateness for HIV positive children. In response to this gap in knowledge, the ACF International Network proposed clinical research, to address the question whether nutritional rehabilitation protocols need to be adapted for HIV infected children. The research looks at the response of malnourished HIV infected children to nutritional rehabilitation and the causes of mortality. The main research question asked was:

> *"To what extent does HIV/AIDS affect a severely malnourished child's response to nutrition therapy?"*

This issue was addressed through a cohort study. As already highlighted, many children do not get tested for HIV during admission in the NRU. One of the things thought to play a role in refusal of HCT is existing stigma around HIV. To be able to better address this problem, it was designed, as part of the research, to include a cross sectional study looking at the stigma around HIV in the context of the NRU to assess the subsidiary research question:

> *"How does HIV/AIDS affect the reported attitudes and behaviours of staff towards children and their carers in the NRU?"*

### Study design

Many children do not get tested for HIV during admission in the NRU. One of the things thought to play a role in refusal of HCT is existing stigma around HIV. To be able to better address this problem, it was designed, as part of the research, to include a study looking at the stigma around HIV in the context of the NRU.

The recruitment of a cohort of children started in May 2005 in three NRU in the central region of Malawi: Kamuzu Central Hospital, Mitundu Community Hospital and St Gabriel's Hospital.

Out of 507 children recruited to the study, data from 454 children was analysed. Baseline characteristics collected included age, sex, HIV status and CD4%, haemoglobin level, presence of oedema, malaria status, maternal health factors and location of residence.

Inclusion criteria:

- Admitted to NRU with <70% weight/height or bilateral oedema
- Agreement by carer to stay for full length of treatment until 85% weight/height
- Age 6 months – 5 years
- Agreement by mother or guardian for HIV testing for self and child

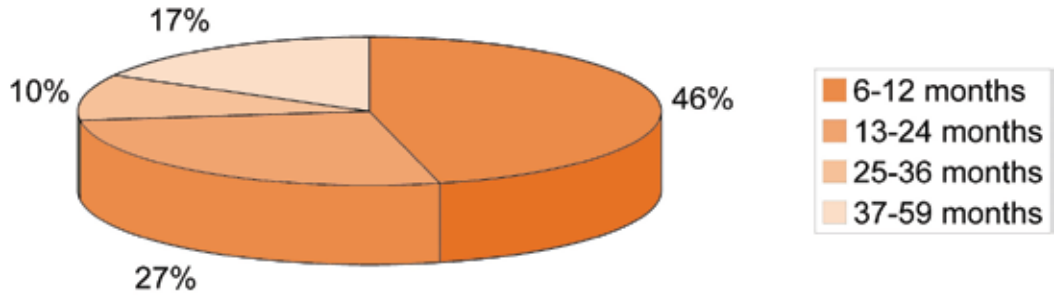
## Results

HIV infected severely malnourished children in Malawian NRU were 3.4 times more likely to die than comparable uninfected children.

Of the 454 children, HIV prevalence was 17.4% and there was 14.8% mortality overall. 35.4% of the HIV infected children died, compared with 10.4% of the HIV uninfected children; this gap was statistically significant. HIV infected children were also significantly more likely to have low haemoglobin and to live in an urban household. They were less likely to be oedematous or to have malaria.

Mortality in the HIV negative children varied by NRU, and was less than 10% in two NRU complying with acceptable international standards[33]. Mortality among the HIV infected children was considerably higher than acceptable international standards in all three NRU, ranging from 20-38.5%. Younger children were more likely to die, with those aged between 6-12 months having the highest prevalence of mortality, as shown in figure 3.

Figure 3 Mortality among HIV positive children enrolled in NRU






HIV infected children were not more likely than HIV uninfected children to die within the first 48 hours or at home during the four month follow-up period after nutritional recovery and discharge. More than 50% of deaths within the hospital occurred by day 10. Of the 83.6% (56/67) mortality that occurred in hospital, 75% of them had been transferred from the NRU to the paediatric ward. 16.4% of deaths occurred at home during the follow up period after discharge from nutrition rehabilitation. Figure 4 gives a summary of all mortality.

Figure 4 HIV prevalence and mortality by site

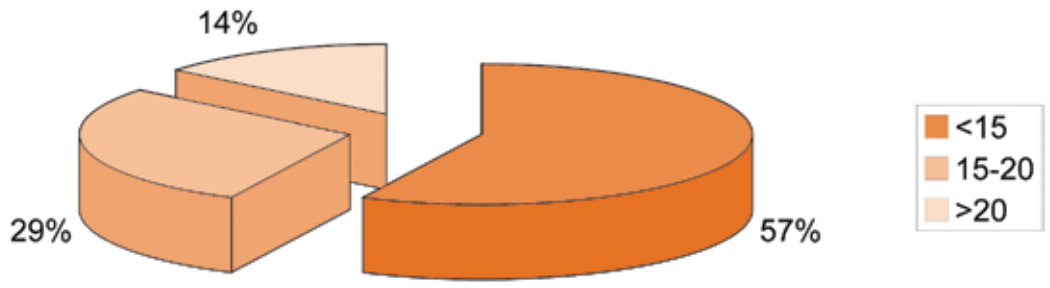
| NRU | HIV prevalence | Mortality in hospital HIV uninfected | Mortality in hospital HIV infected | Mortality in hospital overall | Mortality during home follow-up | Mortality overall (including follow-up) |
|---|---|---|---|---|---|---|
| KCH | 36.3% (61/168) | 6.5% (7/107) | 29.5% (18/61) | 14.8% (25/168) | 1.8% (3/168) | 16.7% (28/168) |
| Mitundu | 4.5% (5/110) | 2.9% (3/105) | 20% (1/5) | 3.6% (4/110) | 3.6% (4/110) | 7.3% (8/110) |
| St Gabriel's | 7.4% (13/176) | 13.5% (22/163) | 38.5% (5/13) | 15.3% (27/176) | 2.3% (4/176) | 17.6% (31/176) |
| Total | 17.4% (79/454) | 8.5% (32/375) | 30.4% (24/79) | 12.3% (56/454) | 2.4% (11/454) | 14.8% (67/454) |



### Levels of immune status

CD4% results were available for 374 children. 53.8% (35/65) of HIV infected children had a CD4% of less than 15%, as compared to only 0.97% (3/309) in HIV uninfected children. 85.7% of deaths in HIV infected children occurred in children with CD4 below 20%.

Figure 5 Mortality by CD4%






HIV infected children with a CD4% below 20% were significantly more likely to die than HIV infected children with CD4% above 20%.

40% (18/45) of HIV infected children with a CD4% under 20 died, in contrast to 15% (3/20) of HIV infected children with a CD4% over 20.

Using the 2006 WHO recommendations for paediatric ART by CD4%[34], 69.2% (45/65) of the HIV infected children in our study with SAM required ART. None of these children were receiving ART upon admission to the NRU. One third of the children requiring ART died while still in the NRU.

## Discussion

This study shows clearly that mortality was markedly increased in HIV infected children compared with HIV uninfected children, and this occurred despite 24 hour medical and nutritional care. Internationally accepted minimum standards for treatment of SAM state that mortality should be within 10% in a therapeutic feeding programme[35]. While the overall mortality of 12.3% (within the hospital) or 14.8% (including follow-up) does not meet this standard, it is valuable to further break down the cohort by facility and HIV status. Both KCH and St. Gabriel's hospitals are referral hospitals that receive transfers of complicated cases from across the region. At KCH, over one third of the children with SAM were HIV infected. The mortality among HIV uninfected children is within SPHERE minimum standards at 8.5% demonstrating acceptable quality of care, but the overall mortality at the centre is elevated above this benchmark by the high rates of mortality in complicated malnutrition amongst the HIV infected children. The high incidence of mortality among the HIV infected children in this cohort cannot be explained by poor quality of nutritional care but rather indicates the high rate of medical complications in the HIV infected children. Indeed, this rate of mortality in the HIV infected children suggests that minimum standards, devised for the emergency context, need to be revised for use with children with complicated SAM in the context of HIV.

One of the limitations of the study is that HIV results were not known for 13% (67/507) of the patients, either because they died before having an HIV test, or because their blood sample was clotted or their result missing from the lab. Data from some of the most vulnerable children will therefore have been lost during this early period. As there was one-third mortality in this group, more than double that of the hospital mortality within children recruited to the study, it is also probable that a higher proportion of these children were HIV-infected.

While 75% of hospital deaths occurred on the paediatric ward, this is not an indictment of quality of care on the wards, but rather a demonstration of the complications seen by hospitals in HIV related SAM. We were not able to assess precise cause of death in these children, but this finding highlights the need for continuity of nutrition therapy and medical care though collaboration between medical paediatric care and nutrition rehabilitation programmes where the two systems are separate.

CD4% criteria for commencing ART in children with SAM need to be urgently examined and clearly defined. More than half of all HIV infected children with SAM had a CD4% below 15%, and low CD4% was a high risk factor for mortality. While the majority of deaths occurred in children with a CD4% <15, an important proportion of mortality also occurred in children with CD4% between 15 - 20%. Overall, nearly 70% of HIV infected children with SAM in the cohort required ART according to WHO criteria supporting the inclusion of SAM as a staging criterion for ART initiation.

HIV infection greatly increases mortality in children with SAM even in nutrition rehabilitation programmes with good quality of nutritional and medical care. While improvement in care practices and adherence to guidelines for the treatment of SAM have been shown to decrease mortality [36,37], this data shows that the complexity of case presentation also affects mortality rates.

The 2004 WHO literature review of current practice in the treatment of severe malnutrition identified several priority areas for further research; including effectiveness of ART in children with SAM, and the level of immunosuppression and phase of malnutrition treatment to begin ART[38]. The 2006 paediatric WHO ART guidelines for resource limited settings state that expert opinion suggests children with SAM should be stabilised on nutritional treatment with return of appetite before ART is initiated[39] (WHO 2006). The question remains as to what extent ART initiated in children with complicated cases of SAM will be effective in preventing mortality, due to the concentration of advanced cases with late presentation.

## Lessons for community based management

Over 50% of mortality occurred within the first 10 days after hospital admission. This highlights the complexity of the medical management of complicated malnutrition and emphasises the standards of care and optimal medical treatment that have been striven for over the last decades[40]. It is essential that this is not forgotten in the 'public heath approach' of the community-based model and that the correct management of clinical care is still given the importance and training that is warranted for the stabilisation centres. Another point to note is the similarity in the incidence of mortality between the HIV infected and uninfected in the early stages of treatment when complications still preside, and then again after recovery during follow up. Overall, the HIV infected children had a three times higher risk of dying. If the risk was not higher in the early stages, and similar after nutritional recovery, it suggests that the higher risk lies in the treatment phase, after stabilisation and before recovery. Several possible explanations could be proposed: inappropriate management of HIV related complications in the stabilisation phase; risk of hospital acquired infections in children with poor immunity; and finally, it perhaps questions the suitability of milk-based protocols on a chronically HIV-affected gut. Further analysis on morbidity will be needed to answer such questions. However, comparisons with HIV infected children in community-based models would certainly be valuable.

37.7% of HIV infected children requiring ART within this study died before achieving nutritional recovery and therefore before the chance to start ART post HIV diagnosis. This emphasises the urgent need for HIV screening services to be more widely accessible to all potentially exposed children. PMTCT programmes, which are scaling up in Malawi, provide an ideal opportunity for this. HIV exposed children should be followed up, and tested for HIV through specialised infant tests or antibody testing. Timely and adequate care and treatment can then be offered to those children found to be HIV infected, which can prevent development of irreversible damage to their health and development. Also, in those children with signs of malnutrition and faltering growth, detection and treatment of HIV should be a priority, the earlier the better. This must involve all health care workers who see children, and the integration of HIV detection and care into the Malawi IMCI guidelines is a good step towards this. Waiting until children develop SAM puts them at unnecessary high risk of mortality. We urgently recommend that all inpatient and community based programmes for the treatment of both moderate and severe malnutrition in high HIV prevalence areas include testing and counseling for HIV.